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14. ABSTRACT

Currently amputation, arthrodesis (joint fusion), or joint replacement are used to treat a joint with an intra-articular fracture or destroyed by a combat injury. Generation of personalized, anatomically shaped biological implants formed using techniques of regenerative medicine in conjunction with biodegradable biomaterial structures to restore a damaged articular joint surface to normal tissue structure, form and function is one way to overcome the limitations associated with current treatment methods. The aims of this study are to: 1) identify the parameters that generate anatomically shaped bone substitutes of optimal composition and structure with an articulating profile. 2) to develop a source of human chondrocytes that can generate sufficient amounts of a cartilage layer to cover the bone substitute; and 3) to evaluate the structures formed in a preclinical model. The ongoing studies will further our understanding of the regulation of cell differentiation to chondrocytes and the bone substitute properties required to form a biological joint replacement.

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Table of Contents

INTRODUCTION

The complexity of extremity injuries as a consequence of battlefield trauma requires multifaceted reconstructions and has resulted in the need to develop entirely new treatment options to achieve limb salvage and thus full rehabilitation. **The overall aim of this research project is to evaluate, using an animal model, large anatomically shaped biological implants formed using techniques of regenerative medicine in conjunction with biodegradable biomaterial structures to restore a damaged articular joint surface to normal tissue structure, form and function prior to progressing to clinical trials to evaluate the application of this treatment approach to humans.** Our multi-disciplinary team is focusing on generating medial tibial plateau and a large segment of the medial femoral condyle (knee joint) biphasic implants (definitive care of battle injuries). The approach we will develop will result in an implant that can be customized contoured to replace the portion of the knee joint disrupted either by an intra-articular fracture or trauma. Being able to generate personalized implants is a critical feature given that most combat injuries are irregularly shaped.

Using an approach that allows for the formation of living tissues for joint reconstruction offers the advantage of functional tissue integration as well as adaptation to loading conditions during use which should avoid implant failure that can result from the fatigue or wear of synthetic biomaterial. Furthermore once we develop the conditions it will be possible to generate an implant of any contour, making this approach particularly appropriate for individuals who have irregular-shaped defects as a result of a combat injury. Two issues that must be overcome before these large biphasic constructs can be used clinically, particularly in the military setting, are the identification of an accessible human cell source to generate a large quantity of cartilage tissue and the methodology to easily, rapidly and reliably generate custom-made CPP bone substitutes of desired shape. This report will describe our results to date (year 2 since grant funding obtained).

As this project is entirely interwined and interdependent my annual report is identical to Dr. Rita Kandel (Toronto, Ontario, Canada) and so we have submitted one annual report. Please refer to her report for information.